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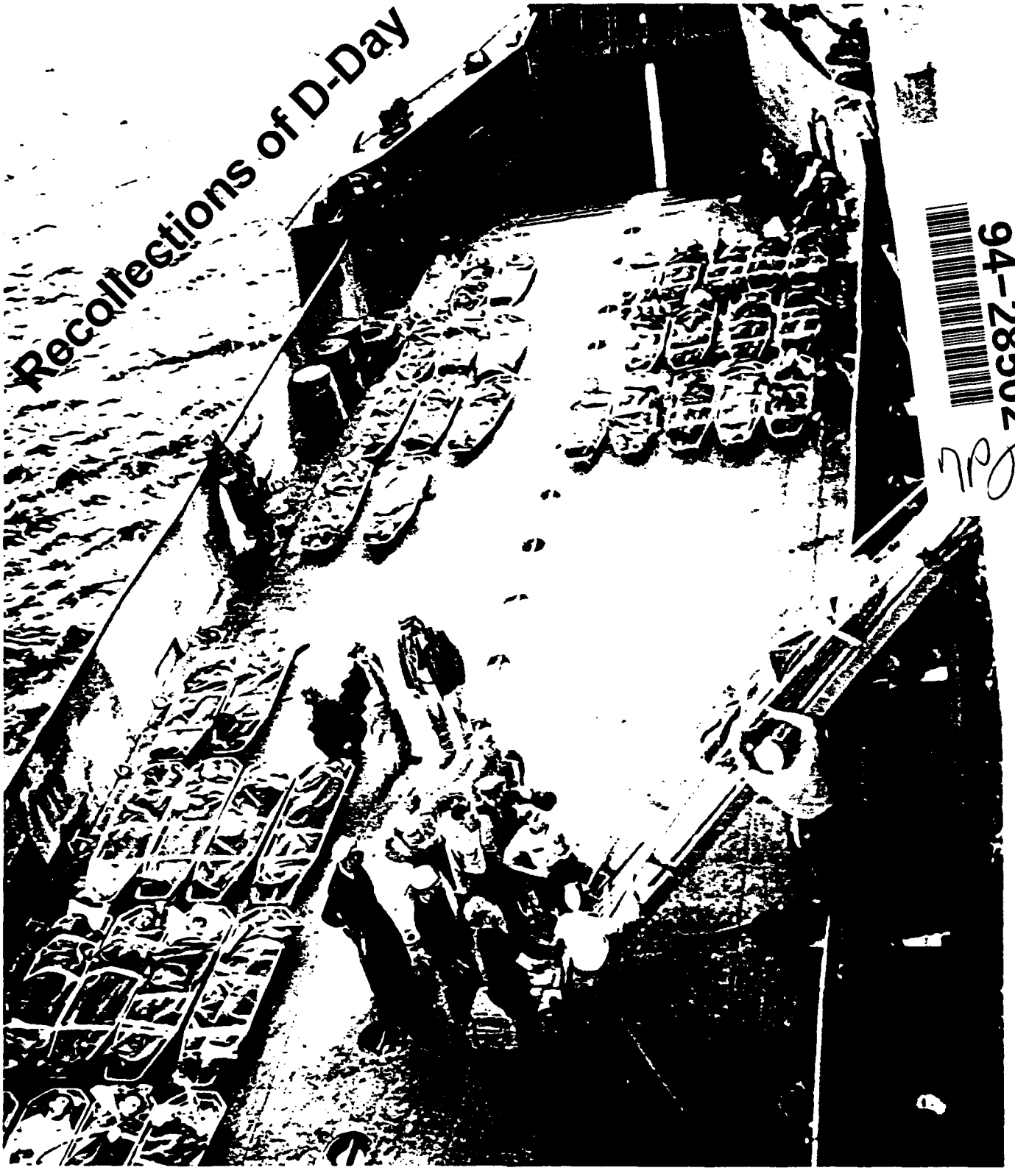

Preventing Malaria

Part 2 of Somalia and General Slim

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Part 1 appeared in March-April 1994.

Malaria discipline refers to the multicomponent program of preventing malaria. It involves the use of personal protective measures and chemoprophylaxis as well as ongoing monitoring and enforcement.

Personal Protective Measures*

If mosquitoes can't bite you, you can't get malaria. Table 1 shows the methods of protection from biting insects. These methods will also protect against many other mosquito-borne diseases, such as dengue fever and Japanese encephalitis, as well as diseases spread by other arthropods such as ticks and biting flies. They should be employed to the fullest extent practicable in the operational setting.

Methods of avoidance of arthropods include choosing bivouac sites that are dry and uncluttered, avoiding rodent burrows and animal pens, and limiting contact with indigenous human populations since they may serve as reservoirs of disease.

Physical barriers include the proper wearing of clothing and the use of protective equipment, such as head nets, bed nets, insect repellent parkas, and tent screens. Proper wearing of clothing reduces the amount of exposed skin and includes tucking the pant leg into boot or sock, rolling

TABLE 1
Methods of Protection Against Mosquitoes and Other Biting Insects

1. Avoidance of arthropod habitats
2. Physical barriers
Proper clothing
Bed nets
Head nets
3. Repellents
DEET
Permethrin
4. Mechanical modifications
Drain standing water
Clear litter and underbrush
5. General sanitation
Proper disposal of trash and waste
6. Pesticides

Reference: *U.S. Army Environmental Hygiene Agency Technical Guide No. 174* (June 1991) (Personal Protective Techniques Against Insects and Other Arthropods of Military Importance)

*An excellent reference for more in-depth information on personal protective measures, including supplies and procedures, is the *U.S. Army Environmental Hygiene Agency's Technical Guide No. 174* (Personal Protective Techniques Against Insects and Other Arthropods of Military Significance) which may be obtained by contacting 410-671-3613/3677, DSN 584-3677, or Aberdeen Proving Ground, MD 21010-5422.

down sleeves, closing the collar, and wearing undergarments and a cap. For malaria prevention it is most important to do this at sunset. These recommendations may not be practical in hot, humid environments.

Since the time of highest risk for malaria transmission is at night, proper use of bed nets is an essential component of malaria prevention. The net should be erected so as to prevent contact of the net with the sleeping person and tucked in around the mattress or cot to preclude entry of arthropods. Added protection can be achieved by treating the bed net with permethrin. This will protect against arthropods small enough to fit through the mesh of the net (e.g., sandflies, midges) and will also prevent insects from biting through the mesh to skin in contact with the net. The treatment should be effective for several months if not rinsed out. The insecticide aerosol 2 percent d-phenorthin can be used to kill mosquitoes inside bed nets and tents. Keeping lighting to a minimum at night will avoid attracting insects.

Arthropod repellents can be used on the skin (DEET) or fabrics such as clothing, bed nets, or tents (permethrin). DEET is a vapor active repellent and works very well for insects such as mosquitoes which bite exposed skin or through light weight clothing. The DEET formulation currently recommended for military use is the 33 percent extended duration cream. This provides protection for 6-12 hours, depending on environment. Permethrin, a contact repellent which is also toxic to arthropods, provides better protection against arthropods which crawl underneath clothing in addition to biting exposed skin, such as sand flies, biting midges, ticks, chiggers, and fleas. Uniforms impregnated with permethrin have been shown to provide almost 100 percent protection against tick bites after five washings and that even after 50 cold water rinses permethrin impregnated fabric killed 100 percent of mosquitoes and ticks.(1) For clothing treated with the aerosol spray, the current recommendation is to reapply after 6 weeks or the sixth laundering, whichever comes first. Dry cleaning completely removes permethrin. Clothing application of permethrin alone ordinarily does not protect exposed skin since there is very little vapor action. Consequently, both DEET and permethrin are required to provide maximum protection. If permethrin is not available, DEET may be applied to clothing to obtain additional protection. The effectiveness of repellents may vary among arthropod species in different parts of the world. Avon Skin So-Soft is a bath oil which is often used as an insect repellent. Laboratory testing found that although it did repel mosquitoes for a short time, it was neither as effective nor as persistent as DEET(1) and it is not recommended for military use.

Mechanical modifications may be used to eliminate mosquito breeding sites, such as draining standing water when possible and preventing water from accumulating in containers and ground depressions. General camp sanitation decreases feeding and hiding sites not only for insects but for rodents which may serve as reservoirs of disease. Pesticides can be very effective in controlling arthropods in certain situations, but should only be employed by persons trained in their use. Information concerning the use of pesticides and other entomology concerns can be obtained by contacting the entomology departments of the Navy Environmental and Preventive Medicine Units.

Chemoprophylaxis

The other component of malaria prevention is the use of drugs to kill the organism once it has gained access to the body but before it can cause illness. Remember that malaria has two developmental phases in the body—one in the liver (which is asymptomatic) and the other in the

Reported Malaria Cases in U.S. Navy and Marine Corps Personnel, February 1988 to May 1993, Excluding Somalia (N = 210)

Service		Area of Disease Acquisition	
U.S. Navy	63	Western Pacific/SE Asia	173
USMC	147	Philippines	145
		Other	28
Type Command		Africa	24
USMC Pacific	131	Other	13
USMC Atlantic	14		
Surface Forces Pacific	22	Species	
Surface Forces Atlantic	5	*P. falciparum*	53%
Air Forces Pacific	2	*P. vivax*	60%
Air Forces Atlantic	4	*P. ovale*	1%
Other	32	*P. malariae*	1%
		Mixed	9%
		Unspeciated	86%

Cases reported to Navy Environmental and Preventive Medicine Units by Disease Alert Reports

blood—and that drugs that work against the blood phase don't work against the liver phase, and vice versa.

Rationale for Chemoprophylaxis. Malaria chemoprophylaxis always involves the use of a blood schizonticide (e.g., mefloquine, doxycycline, or chloroquine) and usually a tissue schizonticide (primaquine) as well. The blood schizonticide is begun prior to the exposure (2 weeks for chloroquine and mefloquine, and 2 days for doxycycline) and continued for 4 weeks after the exposure has ended. Beginning the drug prior to exposure serves two purposes—it allows time to achieve effective blood levels and also to determine if the person can tolerate the medication. The drug is continued for 4 weeks after the exposure (referred to as terminal prophylaxis) in order to maintain a drug level adequate to kill any organisms which emerge from the liver after the person has left the area. For example, if a person is bitten by an infective mosquito just prior to leaving, the organisms will be in liver cells, and therefore unaffected by blood schizonticides, for the next 1-3 weeks. If there is no drug in the blood when the organisms emerge from liver cells, the person will become ill. Additionally, if there has been a risk of exposure to one of the species which forms hypnozoites, *P. vivax* and *P. ovale*, then a tissue schizonticide (primaquine) is also needed after leaving the area to eradicate these forms in the liver. Although the risk varies geographically, Haiti and the Dominican Republic are the only malarious areas with no known risk of *P. vivax* or *P. ovale*.

Drug Resistance. Malaria chemoprophylaxis is becoming more difficult due to increasing prevalence of drug resistant *P. falciparum*. Resistance to chloroquine is confirmed or probable in all countries with falciparum malaria except Haiti, the Dominican Republic, Central America west of the Panama Canal, Egypt, and most of the Middle East. Resistance to chloroquine and Fansidar is present in parts of SE Asia, sub-Saharan Africa, and the Amazon basin area of South America. Mefloquine resistance is prevalent in Thailand along the borders with Cambodia and Burma and has been reported from Africa and Indonesia. Chloroquine resistant *P. vivax* has recently been discovered on the island of New Guinea.

Current Chemoprophylactic Regimens. For naval personnel deploying to malarious areas, one of three regimens may be used, depending on local resistance patterns and potential for adverse effects. Navy personnel should contact the appropriate NEPMU for the most current recommendations.

(1) Mefloquine 250 mg, once per week, beginning 2 weeks prior to entering malarious area and continuing until 4 weeks after leaving.

(2) Doxycycline 100 mg, once per day, beginning 2 days prior to entering malarious area and continuing until 4 weeks after leaving.

(3) Chloroquine phosphate 500 mg, once per week, beginning 2 weeks prior to entering malarious area and continuing until 4 weeks after leaving.

If primaquine is needed, which it usually is after military operations, it may be given either 15 mg (one tablet) per day for 14 days, or 45 mg (3 tablets in a single dose) per week for 8 weeks. Because of the potential for hemolysis, primaquine is generally not given to persons who are G6PD deficient. The daily regimen may be given anytime during the 4-week period in which the person is taking terminal prophylaxis with the blood schizonticide. Primaquine resistant *P. vivax* occurs, but the frequency is unknown. Several possible cases were seen in persons after returning from Somalia. The resistance is usually relative as most persons who fail the 15 mg/day for 14 days regimen will respond to retreatment with 30 mg/day for 14 days.

Chloroquine has few side affects but its use is restricted due to widespread resistance. Mefloquine is effective in most areas and has the advantage of a weekly dosing schedule. Although side effects are associated with the treatment dose of mefloquine, a recent study showed the weekly prophylactic dose to be as safe as chloroquine.(2) The recent Somalia experience revealed the importance of the 2-week pre-exposure dosing of mefloquine for achievement of protective blood levels. It was recently shown that a 3-day loading dose (250 mg/day) achieves effective blood levels more rapidly than the 2-week regimen.(2) At present, general Navy policy remains to begin mefloquine 2 weeks prior to exposure. However, the 3 day loading dose may be indicated in some situations, such as rapid deployments to highly malarious areas in which there is not enough time to complete the 2-week course. Side effects may be more common with this regimen. Mefloquine is the most expensive of the regimens.

Doxycycline is similarly effective in most parts of the world and is the preferred regimen along the borders of Thailand where mefloquine resistance is prevalent. However, it must be taken daily, making compliance more difficult, and side effects are common, especially GI upset. If doxycycline is used it is very important to take it with food to decrease incidence of GI problems. This applies to the other chemoprophylactics as well.

Chloroquine is the only malaria chemoprophylactic available in the United States approved for use in pregnancy. Although not currently approved for such use, no adverse outcomes have yet been associated with the use of mefloquine during pregnancy.

None of the above regimens are 100 percent effective in preventing falciparum malaria in all parts of the world. Because of widespread resistance, cases may be seen even if the medications are taken exactly as prescribed.

For more detailed information on the use and side effects of these drugs, consult the Navy Medical Department Guide to Malaria Prevention and Control.

Preparing for Malaria

It is obvious that malaria prevention is no simple task, especially when dealing with it for the first time. The following guidelines should help the operational medical officer and corpsman prepare for deployment to a malarious area.

1. Know the Risk. The first thing to do is to determine if malaria is a threat and, if so, what chemoprophylactic regimen is recommended. The best source of that information in the Navy is the Navy Environmental and Preventive Medicine Units (NEPMUs) and their country specific disease reports, Disease Risk Assessment Profiles (DISRAPS). Because malaria risk and chemoprophylaxis recommendations can change rapidly, it is always best to consult with an NEPMU prior to deployment. Table 3 gives information on how to contact the NEPMUs. Another excellent source of information about malaria and other travel-related issues is the Center for Disease Control's Health Information for International Travel (HHS Publication No. CDC 93-8280) and may be ordered from the Government Printing Office, Washington DC 20402, (202) 783-3238.

2. Inform the Commanding Officer. It is imperative that you have support for malaria prevention efforts from your command. This must start at the top and be passed down through the chain of command. Line officers must understand the potential of malaria to adversely affect operational readiness.

3. Educate Command in Malaria Discipline. Try to increase individual motivation for complying with malaria discipline by educating forces about the risk and consequences of disease (i.e., falciparum malaria is a potentially fatal disease) and about the means of prevention.

4. Assemble Needed Supplies. Many supplies are needed for the prevention, diagnosis, and therapy of malaria. Predeployment preparation is necessary to prevent later shortcomings. Things to consider include the proper amount of chemoprophylactic medications (for both in-country and terminal prophylaxis), bed nets, DEET, permethrin, and spray insecticide (2 percent d-phenorthrin). For operations in areas with intense insect exposures, head nets and insect repellent parkas may be needed. Also obtain needed diagnostic supplies, such as giemsa stain, and drugs for therapy of malaria cases.

If chloroquine resistance is present, then quinine or mefloquine is indicated for therapy of uncomplicated cases and intravenous quinidine for therapy of complicated, life-threatening infections. Not all the above supplies are generally included as part of routine Authorized Medical Allowance Lists (AMAL). For detailed information about prevention, diagnosis, and therapy of malaria, obtain a copy of the Navy Medical Department Guide to Malaria Prevention and Control.

5. Once Deployed, Monitor and Enforce Malaria Discipline. This is critical, as adherence to preventive measures naturally wanes with time. Take whatever steps are necessary to assure chemoprophylaxis is being taken. It is imperative to involve the chain of command, especially senior

TABLE 3

Navy Environmental and Preventive Medicine Units (NEPMU), With Area of Responsibility (AOR) for Malaria Recommendations

NEPMU-2 (AOR - Central/South America, Caribbean, Iceland)
Naval Station
Norfolk, VA 23511-6288
DSN 564-7671; COM (804) 444-7671; FAX (804) 444-1191
PLAD: NAVENPVNTMEDU TWO NORFOLK VA

NEPMU-5 (AOR - Canada, Mexico, Alaska)
Naval Station, Box 143
San Diego, CA 92136-5143
DSN 526-7070; COM (619) 556-7070; FAX (619) 556-7071
PLAD: NAVENPVNTMEDU FIVE SAN DIEGO CA

NEPMU-6 (AOR - Pacific, SE Asia to India)
Box 112, Naval Station
Pearl Harbor, HI 96860-5040
DSN 471-9505; COM (808) 471-9505; FAX (808) 474-9361
PLAD: NAVENPVNTMEDU SIX PEARL HARBOR HI

NEPMU-7 (AOR - Europe, Africa, Middle East, Russia)
PSC 810 Box 41
FPO AE 09619-4200 (Naples, Italy)
DSN 625-1110, ext. 4470/69; COM (from U.S.) 011-39-81-724-4470/69;
PLAD: NAVENPVNTMEDU SEVEN NAPLES IT

enlisted, in this function. Direct administration of pills is the best way to assure compliance. This is easier with weekly medications. Administer pills after meals to decrease GI complaints. Continue to promote the use of personal protective measures, but realize that some of these may not be practical due to operational or environmental factors.

6. At End of Deployment, Reeducate About Importance of Terminal Prophylaxis. Most malaria cases in recent Navy experience, including Somalia, were due to failure to take terminal prophylaxis. Although the drugs are usually distributed, personnel often fail to comply because they feel they are not at risk for malaria since they are no longer in the country. Postdeployment cases may be decreased by educating personnel about the liver stage of the disease, and, whenever possible, continuing monitoring and enforcement of chemoprophylaxis after leaving the area.

Could It Be Malaria?

Because of the travel associated with military service, Navy medical personnel must always be on the alert for malaria when evaluating a patient with a febrile illness. It should be considered in any patient with a febrile illness and a history of exposure to a malarious area.

Because malaria may occur months to years after the exposure occurred, many persons are far removed from the malarious area when they become ill and only a good travel history will identify malaria as a possible cause. For example, one of the malaria cases from Somalia became ill in Iceland. A history of adequate chemoprophylaxis does not rule out malaria, due to widespread resistance. Although the classic symptoms are fever, chills, headache, and muscle aches, malaria may mimic many other diseases. It should be considered in anyone with a fever and a history of exposure, regardless of what other symptoms are present or absent. Malaria is frequently misdiagnosed as "viral syndrome" and "gastroenteritis."

Until a vaccine or highly effective chemoprophylactic drug are available, which are not on the immediate horizon, malaria will remain one of the most significant threats to military operations. Only by awareness and constant vigilance to preventive efforts can we avoid past experiences, such as those of General Douglas MacArthur who stated in 1943: "This will be a long war if for every division I have facing the enemy I must count on a second division in the hospital with malaria and a third division convalescing from this debilitating disease!"(3)

References

1. *U.S. Army Environmental Hygiene Agency Technical Guide No 174.* Personal protective techniques against insects and other arthropods of military importance. June 1991.
2. Boudreau E, Schuster B, Sanchez J, et al. Tolerability of prophylactic Larium regimens. *Trop Med Parasitol.* 1993;44:257-265.
3. Slim W. *Defeat Into Victory* 2nd ed. London: Cassell & Co; 1956. ❑

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